

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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|--|---|--|
| Applicant's or agent's file reference 09585 | FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | |
| International application No. PCT/JP 03/13901 | International filing date (day/month/year) 30/10/2003 | (Earliest) Priority Date (day/month/year) 01/11/2002 |
| Applicant TAKEDA CHEMICAL INDUSTRIES, LTD. | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 10 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable (See Box I).**

3. ☐ **Unity of invention is lacking (see Box II).**

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 03/13901

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/381 A61K31/4155 A61K31/4174 A61K31/4178 A61K31/4184
A61K31/427 A61K31/4402 A61K31/4439 A61K31/5377 C07D417/10
C07D417/12 C07D403/10 C07D403/12 C07D417/04 C07D231/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, MEDLINE, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| P, X | WO 2003 049702 A (AMGEN INC) 19 June 2003 (2003-06-19) claims and in particular the uses of claim 173; in the description, see in particular compound 212 on page 335 --- | 1, 2, 4-8, 21-28 |
| P, X | WO 2002 098852 A (PIERRE FABRE MEDICATENT, FR.) 12 December 2002 (2002-12-12) examples --- -/-- | 1, 2, 4-8 |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

16 February 2004

Date of mailing of the international search report

04/03/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Elliott, A

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 03/13901

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07F9/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | <p>MONTEIRO, TANIA MARIA ET AL: "Synthesis and analgesic activity of new pyrazole-4-carboxanilides and (E)-3-pyrazol-4-ylpropenylanilides" REVISTA PORTUGUESA DE FARMACIA, vol. 49, no. 4, 1999, pages 153-160, XP009025355 ISSN: 0484-811X figure 4</p> <p style="text-align: center;">--- -/-</p> | 1, 2, 4-8, 23, 27 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

16 February 2004

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Elliott, A

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 03/13901

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | BRATENKO, M. K. ET AL: "Functionally Substituted 3-Heterylpyrazoles: XI. 3-(3-Aryl(heteryl)pyrazo 4-yl)propenoic and Propanoic acids" RUSSIAN JOURNAL OF ORGANIC CHEMISTRY (TRANSLATION OF ZHURNAL ORGANICHESKO KHIMII), vol. 38, no. 8, 2002, pages 1171-7, XP009025357 ISSN: 1070-4280 compounds VI-f & VII-d-f | 1,2,4-8 |
| X | WO 2000 075120 A (AGOURON PHARMACEUTICALS, INC., USA) 14 December 2000 (2000-12-14) page 282, 3rd compound from the bottom page 296, bottom compound page 375, middle compound | 1,4,6,8 |
| X | EP 1 148 053 A (ONO PHARMACEUTICAL CO) 24 October 2001 (2001-10-24) page 81, paragraph 181 | 1,4,6,8 |
| X | PATENT ABSTRACTS OF JAPAN vol. 1998, no. 12, 31 October 1998 (1998-10-31) & JP 10 195063 A (DAI ICHI SEIYAKU CO LTD), 28 July 1998 (1998-07-28) abstract | 1,2,4-8 |
| X | OHTA, MITSUAKI ET AL: "Novel 5-hydroxytryptamine (5-HT ₃) receptor antagonists. I. Synthesis and structure-activity relationships of conformationally restricted fused imidazole derivatives" CHEMICAL & PHARMACEUTICAL BULLETIN, vol. 44, no. 5, May 1996 (1996-05), pages 991-999, XP001179262 ISSN: 0009-2363 compounds 6 & 9 and unsaturated intermediate used in 9's preparation | 1,4,6,8 |
| X | US 5 464 860 A (LEPAGE, FRANCIS ET AL) 7 November 1995 (1995-11-07) table II, compound 9 | 1,2,4-8 |
| X | US 5 250 504 A (MARAVETZ, LESTER L.) 5 October 1993 (1993-10-05) table 1, compounds 46 & 47 | 1,2,4-8 |
| X | US 4 835 280 A (MARTENS, ALFRED ET AL) 30 May 1989 (1989-05-30) examples 18F, 19C | 1,2,4-8 |
| | -/- | |

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 03/13901

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | ZHANG, YUENLANG ET AL: "Chemotherapeutic studies on schistosomiasis. XXXIII. Synthesis of beta-(5-nitroimidazol-2-yl) acrylamides and related compounds" YIYAO GONGYE (PHARMACEUTICAL INDUSTRY), vol. 17, no. 10, 1986, pages 444-8, XP009025354 ISSN: 0255-7223 compounds F-31142, F-31144, F-31145, 40001, 40004 & 40005 --- | 1,4,6,8 |
| X | EP 0 153 850 A (SAWAI PHARMACEUTICAL CO., LTD., JAPAN) 4 September 1985 (1985-09-04) page 23, compound 6 page 19, example 3 --- | 1,4,6,8 |
| X | US 4 172 136 A (BERGER, HERBERT ET AL) 23 October 1979 (1979-10-23) examples 10,12,15 --- | 1,2,4-8 |
| X | US 3 702 330 A (HOFF, DALE R. ET AL) 7 November 1972 (1972-11-07) examples 6,7,10 --- | 1,4,6,8 |
| X | LING Y Z ET AL: "17-Imidazolyl, pyrazolyl, and isoxazolyl androstene derivatives. Novel steroidal inhibitors of human cytochrome C17,20-lyase (P450(17 alpha))." JOURNAL OF MEDICINAL CHEMISTRY, vol. 40, no. 20, 26 September 1997 (1997-09-26), pages 3297-3304, XP002270332 ISSN: 0022-2623 Scheme 3, step ii --- | 30 |
| X | PLATE R ET AL: "Synthesis and muscarinic activities of 3-(pyrazolyl)-1,2,5,6-tetrahydropyridine derivatives." BIOORGANIC & MEDICINAL CHEMISTRY, vol. 4, no. 2, February 1996 (1996-02), pages 227-237, XP002270333 ISSN: 0968-0896 Schemes 1 and 3 --- -/-- | 30 |

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 03/13901

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | LEE C S ET AL: "Carbon-carbon-linked (pyrazolylphenyl)oxazolidinones with antibacterial activity against multiple drug resistant gram-positive and fastidious gram-negative bacteria." BIOORGANIC & MEDICINAL CHEMISTRY, vol. 9, no. 12, December 2001 (2001-12), pages 3243-3253, XP002270334 ISSN: 0968-0896 Scheme 1, step f --- | 30 |
| X | PLATE R ET AL: "Synthesis and in vitro muscarinic activities of a series of 3-(pyrazol-3-yl)-1-azabicyclo[2.2.2]octane S." BIOORGANIC & MEDICINAL CHEMISTRY, vol. 8, no. 2, February 2000 (2000-02), pages 449-454, XP002270335 ISSN: 0968-0896 Scheme 1, step e --- | 30 |
| X | HARPER R W ET AL: "Leukotriene B4 (LTB4) receptor antagonists: a series of (hydroxyphenyl)pyrazoles." JOURNAL OF MEDICINAL CHEMISTRY, vol. 37, no. 15, 22 July 1994 (1994-07-22), pages 2411-2420, XP002270336 ISSN: 0022-2623 page 2416, column 1, line 15 - line 29 ----- | 30 |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-18, 20-29 (all partially)

Present claims 1-19, 20-29 relate to (products comprising and the use of) an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed.

For the above reasons the search has therefore been restricted to that which the International Search Authority believes to be the essence of the application, namely to compounds where ring A is as defined in claim 1, groups X, Z and Y together form an acylamide linker and R1 is a (substituted) phenylene group. All the preferred compounds of claim 19 are covered by this particular generic group of compounds.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 03/13901

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-18, 20-29 (all partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 03/13901

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 03/13901

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| US 3702330 | A 07-11-1972 | NONE | |